## REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116, because the Amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration because the amendments amplify issues previously discussed throughout prosecution; relates to matters of form rather than substance, because the added language was already present in the claims, and places the application in better form for an appeal should an appeal be necessary. Entry of the Amendment, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116, are thus respectfully requested.

As correctly indicated on the Office Action Summary, claims 1-4, 6-7, 9-10, and 17-64 are pending and rejected. The Summary indicates that claims 58-60 have been withdrawn by the Examiner from consideration. Applicants note that Claims 51-53 and 55-57 appear free of prior art.

By this Amendment, Applicants have amended claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57 without prejudice or disclaimer as to the subject matter contained therein. Applicants have canceled claims 28 and 30-32 without prejudice or disclaimer as to the subject matter. Claims 58-60, which were withdrawn from consideration by the Examiner, have also been canceled without prejudice or disclaimer in complete response to the outstanding action. Applicants reserve the right to file a continuation or divisional application on any subject matter canceled by way of amendment.

The amendments to the claims are provided at least in the claims as originally filed and throughout the specification and as discussed more fully below. The amendments have been introduced to more clearly and distinctly claim the subject matter. Support for the new claim 65 can be found at least in original claim 55.

Claims 1-4, 6-7, 9, 10, 17-27, 29 and 33-57 have been amended to recite "The method" instead of "Method". Certain claims have also been amended to recite "tissue" instead of "tissue section" or "tissue sample" to more clearly and distinctly claim the subject matter (*i.e.*, claims 1-3, 24, 25, 26 and 29). The claims have been additionally amended by

removing the phrase "characterized in that" as suggested by the Examiner (*i.e.*, Claims 2, 3, 6, 7, 9, 10, 17-22, 25-27 and 29-67). These amendments are supported at least by the claims as originally filed.

Support for the amendments to claim 1 can be located in the specification at least at page 4, line 28 to page 5, line 4, in the Examples at page 9, line 3 *et seq.* and in the claims as filed. The term "mounted" is supported at least at page 8, line 6. The first instance of the phrase "*in vivo*" has been removed from the claim to more clearly claim the subject matter. A cleavage step is also now recited in claim 1. These latter amendments are supported at least by the claims as originally filed.

The amendment to Claim 2 is supported by the specification at least at page 6, lines 8-14, and in the Examples and in the claims as originally filed.

The amendment to Claim 3 is supported by the specification at least at page 6, lines 8-14, page 16, line 10 *et seq.* and the claims as originally filed.

The amendment to Claim 4 is supported by the specification at least at page 5, lines 5-6.

The amendment to Claim 6 is supported by the specification at least at page 5, lines 16-17.

Claims 9, 24, 29, 33, 34, 52 and 53 have been amended to depend on a currently pending claim or to depend from a more appropriate claim give the amendments to the claims.

Claims 6, 7, 17-23, 34 and 57 have been amended to remove the term "displayed" in light of amendments to claim 1. The amendments are supported at least in the claims as originally filed.

The amendment to Claim 22 is supported by the specification at least at page 6, lines 1-7.

The amendment to Claim 24 has been amended to more distinctly claim the subject matter of the invention and is supported at least by original claim 24.

Claim 27 has been amended to recite "a" before several of the enzymes for parallelism.

Claim 33 has been amended in view of the cancellation of claim 28 and the amendment to claim 1. The amendment is supported at least by claims 1, 28, and 33 as originally filed.

Claims 39-41 have been amended to remove "and/or preselected".

Claims 42, 43, 47, and 54 have been amended to refer to the steps of claim 1 more distinctly. Claim 47 has also been amended by removing "a" before "cleavage".

Claims 44 and 45 have removed "the" before "linkage" to more distinctly claim the subject matter.

Claim 48 and 51 have been amended to more distinctly claim the cleavage process.

Claim 50 has been amended by removing "the" before "minor coat" to more distinctly claim the subject matter.

Claim 55 has been amended to remove "such as triethylamine", which is now recited in new claim 65.

Claims 56 and 57 have been amended by removing "the" and introducing "a" or "an" respectively for appropriate antecedent basis.

In view of the above, Applicants believe that no prohibited new matter is introduced by entry of the above claim amendments and new claim 65.

## I. Rejections Under 35 U.S.C. § 112 (First Paragraph)

Claims 4 and 61-64 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking written description.

***Claim 4.*** Without conceding to the Examiner's arguments and in an effort to expedite prosecution of the application, Applicants have amended claim 4 by omitting "any other homogeneous binding structure", thereby mooting the rejection. Applicants respectfully request withdrawal of the rejection and allowance of claim 4.

***Claim 61.*** Applicants traverse the rejection of claim 61. Claim 61 stands rejected for recitation of "combination of subtractive tissue selections". Respectfully, the specification

need not describe the claimed invention *ipsis verbis* to comply with the written description requirement. *Ex parte* Sorenson, 3 U.S.P.Q. 2d 1462, 1463 (Bd. Pat. App. & Int. 1987). Applicants direct the Examiner's attention to at least page 16, lines 10-21, which describes "negative selection". Multiple selection rounds are discussed, for example, on page 17, line 22. Therefore, Applicants submit that claim 61 is supported by the specification and would place one of ordinary skill in possession of the invention as required. Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of claim 61.

***Claims 62 and 63.*** Applicants traverse the rejection of claims 62 and 63. Claim 62 (and dependent claim 63) stand rejected for recitation of "both positive and negative tissue selections, with different types of libraries". Applicants respectfully direct the Examiner's attention to at least page 13, lines 1-26 (Example 4) which describes positive and negative tissue selections. Different types of libraries are discussed, at least, at page 7, lines 3-8 and see also page 6, lines 12-13. In view of at least the above noted sections of the specification, claims 62 and 63 are amply supported by the specification, and the rejection should appropriately be withdrawn and the claims allowed.

***Claim 64.*** Applicants traverse the rejection of claim 64. Claim 64 stands rejected as allegedly lacking support for the method step of "wherein non-phenotype specific binding structures are removed from the library by means of negative selection against tissues lacking the phenotype comprising said target structures." The Examiner's attention is respectfully directed to at least page 6, lines 11-12 ("A selection system can thus be a combination of a tissue phenotype subtractive approach....") and to the Examples, starting at Example 4 *et seq.* In view of at least these sections of the specification, one of ordinary skill would have understood the claimed invention and thereby had possession. Therefore, Applicants submit that as claim 64 is supported by the specification, the rejection should appropriately be withdrawn and the claim allowed.

## II. Rejections Under 35 U.S.C. § 112 (Second Paragraph)

Claims 1-4, 6-7, 9-10, 17-57, and 61-64 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly describe the claimed subject matter.

***Claim 1.*** The Examiner rejected claim 1, because it is unclear what the claimed means of isolation is and whether isolating the desired structure refers to the binding structure alone or in concert with the target structure. The Examiner also correctly noted the lack of a step (e). Applicants have amended claim 1 such that the preamble and the steps now refer to an "initial" combinatorial phage. Additionally, claim 1 has further been amended to recite step (e). By entry of these amendments to claim 1, the rejection appears mooted and should therefore be withdrawn.

Claim 1 was further rejected for reciting "other identifying information". Without acquiescing to the merits of the Examiner's argument and in an effort to expedite prosecution of the application, the phrase has been removed, thereby mooting the rejection.

On page 4 of the Office Action, it was alleged that the terms "first" and "second library" are unclear. Applicants have amended claim 1 to refer to an "initial library". Additionally, step (c) of claim 1 as amended now more clearly recites what constitutes the second enriched library, namely the bound phage particles which are capable of binding to the target structures. Applicants have also amended claim 1 to refer to *in vivo* and *in situ* targets in the alternative (i.e., "or"). The amendments to claim 1 in view of the teachings of the specification make clear the claimed invention. Therefore, the rejection should accordingly be withdrawn.

Dependent claims 17-21 also stand rejected under § 112, second paragraph for recitation of the term "characterized". Without acquiescing to the Examiner's arguments and in an effort to expedite prosecution, Applicants have amended claims 2, 3, 6, 7, 9, 10, 17-22, 25-27 and 29-57 to remove the term "characterized", thereby mooting the rejection.

Claim 1 was also rejected for lack of clarity regarding *in situ* and *in vivo*. Applicants have amended claim 1 such that it is now clear that the tissue is removed from the subject, and is thus *in situ*. The remaining use of the term *in vivo* regards the fact that the identified phage particles which bind to cells from the tissue would be capable of binding to these cells either *in situ* or *in vivo*. For example, the use of the term *in vivo* as recited in step (e) would mean that the molecule to which the phage particles bind is in its native form as expressed in the host organism.

The Examiner also indicated that Applicants appeared to acquiesce the issue regarding claim 1 and its "recitation of acquiring a binding structure(s). . . ." Office Action, page 4, last paragraph. Applicants assert that the point has not been acquiesced, but in view of the amendments to claim 1, the issue has been mooted.

***Claim 4.*** Claim 4 was rejected as indefinite for recitation of "other homogenous binding structure". The amendment to claim 4 has mooted the rejection, thus Applicants respectfully request withdrawal of the rejection.

***Claim 6.*** The Examiner maintains the rejection of claim 6, as indefinite as to what is meant by "previously uncharacterized, unpurified and unknown molecules" and what the phrase includes. The rejection is moot in light of the amendment to claim 6. Accordingly, Applicants request withdrawal of the rejection.

***Claim 7.*** Claim 7 is rejected as indefinite because the term "displayed" lacks antecedent basis. Applicants have amended claim 7 by removing the first recitation of the term "displayed", thereby mooting the rejection. Withdrawal of the rejection is now in order.

***Claim 22.*** The rejection of claim 22 was maintained as indefinite for recitation of the phrase "a portion and/or a set of antigens." As claim 22 has been amended to no longer recite the phrase, the rejection is moot. Applicants respectfully request withdrawal of the rejection.

***Claim 23.*** Claim 23 stands rejected as indefinite for the recitation of "displayed" and for recitation that the target is a protein. Applicants have removed "displayed" from the claim thereby mooting that rejection. Applicants have also amended claim 23 to "...wherein the target structure comprises a protein, a carbohydrate, a nucleic acid, or a lipid." With the amendments to claim 23, Applicants believe the rejections to be moot. Accordingly, Applicants respectfully request withdrawal of the rejection.

***Claims 24-27.*** Claim 24 and associated dependent claims stand rejected as indefinite because it is allegedly unclear regarding how the method of obtaining of tissue further limits the base claim. More specifically, the claims allegedly lacked antecedent basis for "authentic *in vivo* or *in situ* phenotype."

Applicants have amended claims 9, 24, 29 and 34 so that they no longer depend either directly or indirectly on canceled claim 8. Additionally, Applicants have also amended

Claim 24 such that it no longer recites the rejected phrase. In view of these amendments, Applicants believe that the rejection is moot and should appropriately be withdrawn.

***Claims 30 and 32.*** Claims 30 and 32 stand rejected as indefinite because the difference between "actively" and "passively" secreted secretions remains unclear. Applicants traverse the rejection. Without acquiescing as to what is meant by the terms "actively" and "passively", which would have been clear to the skilled artisan at the time (see, e.g., the attached diagram regarding active and passive transport), the claims have been canceled. In light of the cancellation of claims 30 and 32, the rejection is mooted and can be withdrawn.

***Claim 39.*** Claim 39 remains rejected as allegedly unclear as to the basis of library preselection. In view of the amendments to the claim canceling this language, the rejection is moot. Thus, Applicants respectfully request withdrawal of the rejection.

In view of at least the above arguments and amendments to the claims, Applicants request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph and allowance of the claims.

## III. Rejections Under 35 U.S.C. § 102(b)

Claims 1-4, 6-7, 9-10, 17-50, 54, and 61-64 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over any one of: Tse *et al.* (WO 94/26787); Williams *et al.* (Immunotechnology).

***Tse et al.*** Without conceding to the Examiner's arguments and in an effort to expedite prosecution, Applicants have amended claim 1 to recite the step of direct elution and recovery of the bound and unbound phage particles. Tse *et al.* do not teach or suggest the direct elution of phage particles, as conceded by the Examiner. As Tse *et al.* do not teach or suggest all the elements of the claims as amended, at least with respect to the step of direct elution, the reference cannot anticipate or render obvious the claimed invention. Accordingly, Applicants respectfully request the withdrawal of the rejection under §§ 102(b) or 103(a) based on Tse *et al.* and allowance of the claims.

***Williams et al.*** Applicants traverse the rejection. As amended, the claims clearly indicate that the tissue obtained from the animals is *in situ*. The phage of the instant invention are not injected into animals *in vivo* as taught and suggested by Williams *et al* (see, page 295 of Williams, first paragraph, lines 8-10). The phage herein are applied to tissue obtaining using histological techniques from the subject organism. Consequently, in view of the amendments to the claims to more clearly and distinctly claim the subject matter of the invention, the reference does not teach or suggest all the elements of the claimed invention as amended. Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

***Cai et al.*** Applicants also note for the record that no further mention was made of the reference by Cai *et al.*, *Proc. Natl. Acad. Sci. USA* 93: 6280-5 (Jun. 1996). Therefore, Applicants' arguments provided in the previous response must have been found persuasive. Accordingly, the rejection of claims 1-50 and 54 under 35 U.S.C. § 102(b) in view of Cai is considered withdrawn.

## IV. Rejections under 35 U.S.C. § 102(e)

Claims 1-4, 6-7, 9-10, 17-50, 54 and 61-64 stand rejected under 35 U.S.C. § 102(e) as anticipated by, or obvious over, either Ruoslahti *et al.* (U.S. Patent No. 5,622,699) or O'Mahony (U.S. Patent No. 6,117,632) based on the arguments made of record in the prior Action.

***Ruoslahti et al.*** The Office Action asserted that the same arguments as were applied for Williams and Tse are also applied to the reference by Ruoslahti *et al.* Applicants traverse the rejection in the event that it applies to the amended claims. Applicants note that like Williams *et al.* Ruoslahti *et al.* require *in vivo* panning of a library to identify molecules (see, e.g., col. 4, lines 20 *et seq.*). Applicants invention clearly now recites that the tissue is *in situ*. Accordingly, given that the same arguments are applied, then the claims should similarly not be anticipated or rendered obvious in view of the amendments to the claims. Applicants therefore respectfully request withdrawal of the rejection and allowance of claims 1-4, 6-7, 9-

10, 17-50, 54 and 61-64 for at least the same reasons as discussed above for Williams and Tse.

***O'Mahony.*** Claims 1-4, 6-7, 17-50, 54 and 61-64 remain rejected in view of U.S. Patent No. 6,117,632 issued to O'Mahoney under 35 U.S.C. § 102(e). Applicants traverse the rejection for at least the reasons made of record in the prior response, as well as for the reasons set forth below. First, O'Mahoney patent is distinguishable from the claims as amended, because this patent requires that the tissue be treated with current (see *e.g.*, col. 12, lines 1-34, especially lines 27-29). In contrast, Applicants' claimed invention do not require the tissue to be subjected to current. Second, O'Mahoney does not teach or suggest the step of direct elution, as recited by the claims as amended. Third, O'Mahoney cannot mount their tissue, because side orientation of the tissue sample(s) is a required element of their invention (*e.g.*, apical and basolateral cellular orientation as discussed at col. 2, lines 15-22). Mounting the tissue would prevent the study of transported peptides across the tissue or cells. As Applicants have amended claim 1, and all the corresponding dependent claims to reflect that the tissue is mounted to a substrate, it becomes apparent that O'Mahoney in fact teaches away from Applicants' claimed invention, as amended.

Accordingly, for at least these reasons, O'Mahoney neither teaches all the claimed elements, nor suggests the claims as amended. Applicants thus respectfully request withdrawal of the rejection under § 102(e) and allowance of the claims.

## CONCLUSION

In view of the foregoing arguments and amendments, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions to that prosecution of this application may be expedited.

Respectfully submitted,

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Date: November 19, 2001

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

1. (Three Times Amended) A method [Method] for acquiring monoclonal antibodies [binding structure(s)] against a target structure by means of reacting an initial combinatorial phage [a first] library [of binding structure(s)] linked to genetic [or other identifying] information, comprising the steps of:

(a) reacting the [first] initial library with mounted tissue [sections comprising an] of one or more [*in vivo* target structure or an] *in situ* target [structure such that the binding structures of the first library bind to the *in vivo* target structure or the *in situ* target structure] structure(s);

(b) [separating the *in vivo* target structure or the *in situ* target structure and binding structures which bound to the target structure from unbound binding structures; and] eluting directly and recovering the unbound phage particles from phage particles which bound to the target structure(s), wherein the recovered unbound phage particles comprise a first enriched library, not capable of binding to the target structure(s);

(c) recovering the bound phage particles by cleaving said bound phage particles from the cells, and wherein the bound phage particles comprise a second enriched library capable of binding the target structure(s); [or the unbound binding structures; and]

(d) amplifying [the bound or the unbound binding structures to create a second library which is enriched with bound or unbound binding structures] either enriched library; and

(e) purifying individual elements of either enriched library and identifying the desired phage particle(s) which exhibit desired binding behavior *in vivo* or *in situ* against the target structure(s) of interest after steps (a) through (d) [isolating the desired binding structure(s) against a target structure].

2. (Amended) The method [Method] as claimed in claim 1[, characterized in that the] further comprising repeating steps (a) through (c) against tissue, which tissue is positive for the target structure(s), to positively enrich for binding phage particles.

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

3. (Amended) The method [Method] as claimed in claim 1[, characterized in that the] further comprising repeating steps (a) through (d) against further tissue which does not display the target structure(s), effecting a negative enrichment.

4. (Three Times Amended) The method [Method] as claimed in claim 1[, wherein the desired binding structure(s) comprise(s) monoclonal antibody(ies), proteins(s), peptide(s), organochemical entity(ies), or any other homogeneous binding structure] further comprising repeating steps (a) through (d).

6. (Twice Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the [displayed] target structure [includes previously uncharacterized and/or unpurified and/or unknown molecules] is displayed as an authentic cellular epitope.

7. (Three Times Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the [displayed] target is displayed as an authentic phenotypic epitope.

9. (Amended) The method [Method] as claimed in claim [8] 7, [characterized in that] wherein the authentic *in vivo* and/or *in situ* phenotypes [is] are the result of a physiological process, a pathological process, a cell and/or tissue development and differentiation, or a drug response, or a naturally occurring degradation process.

10. (Amended) The method [Method] as claimed in claim 9, [characterized in that] wherein the pathological process is an inflammation, a secondary tumor deposit, or tumor vasculature.

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

17. (Twice Amended) The method [Method] as claimed in claim 7, [characterized in that] wherein the set of [displayed] target structures are target structures from a whole cell.

18. (Twice Amended) The method [Method] as claimed in claim 7, [characterized in that] wherein the [displayed] target structure is located in a cell surface.

19. (Twice Amended) The method [Method] as claimed in claim 7, [characterized in that] wherein the [displayed] target structure is located intracellularly of a cell surface.

20. (Twice Amended) The method [Method] as claimed in claim 7, [characterized in that] wherein the [displayed] target structure is located extracellularly of a cell surface.

21. (Twice Amended) The method [Method] as claimed in claim 7, [characterized in that] wherein the [displayed] target structure is located intranuclear of a nuclear membrane.

22. (Three Times Amended) The method [Method] as claimed in claim 7, [characterized in that] wherein the [displayed] target structure(s) is a simple or complex epitope comprising [comprises the whole and/or a portion and/or a set of (an) antigen(s), (an) epitope(s), (a)] ligand(s), (a) receptor(s), (an) adhesion molecule(s), (a) matrix [molecule(s) and/]or [(a)] matrix-associated-molecule(s), other than luminal vasculature targets [and/or a portion and/or a set thereof].

23. (Twice Amended) The method [Method] as claimed in claim 22, wherein the [displayed] target structure [is based on] comprises a protein, a carbohydrate, a nucleic acid, or a lipid.

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

24. (Three Times Amended) The method [Method] as claimed in claim [8] 1, wherein the tissue [section with the authentic *in vivo* or *in situ* phenotype] is obtained by a histological technique.

25. (Amended) The method [Method] as claimed in claim 24, [characterized in that] wherein the histological technique comprises freezing and/or fixation, and sectioning of the [a] tissue [sample].

26. (Amended) The method [Method] as claimed in claim 24, [characterized in that] wherein the tissue [sections are] is pre-treated with enzyme or by chemical means.

27. (Amended) The method [Method] as claimed in claim 26, [characterized in that] wherein the enzyme pre-treatment is performed with a protease and/or a polysaccharase and/or a ribonuclease, and/or a nuclease.

29. (Amended) The method as claimed in claim 1, wherein the [body fluids] tissue is [comprise blood,] a suspension of bone marrow cells, lymph cells, sperm cells, or cells from cerebrospinal fluid[, or secretions from cells].

33. (Amended) The method as claimed in claim 1, wherein the *in situ* target comprises cells suspended from the tissue [body fluids are suspended cells from a tissue or pelleted cells from a body fluid].

34. (Twice Amended) The method [Method] as claimed in claim [8] 1, [characterized in that] wherein the [displayed] target structure is a molecule released from cells.

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

35. (Amended) The method [Method] as claimed in claim 34, [characterized in that] wherein the cells are tumor cells.

36. (Amended) The method [Method] as claimed in claim 34, [characterized in that] wherein the molecule is released actively.

37. (Twice Amended) The method [Method] as claimed in claim 34, [characterized in that] wherein the molecule is released passively.

38. (Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the [first] initial library is a naive, synthetic, or semi-synthetic antibody library.

39. (Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the [first] initial library is a combinatorial [and/or preselected] library.

40. (Amended) The method [Method] as claimed in claim 39, [characterized in that] wherein the combinatorial [and/or preselected] library is a library produced by immunization against one or more displayed target structures.

41. (Amended) The method [Method] as claimed in claim 39, [characterized in that] wherein the combinatorial [and/or preselected] library is a chemical library.

42. (Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the step of acquiring [acquirement of] binding structures further comprises identifying, producing, characterizing, selecting, enriching, or defining such structures.

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

43. (Twice Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the step of amplifying [amplification of] bound binding structures further comprises amplifying the bound binding structures using bacterial cells, PCR synthesis or chemical synthesis [synthesis in growing bacterial cells, PCR synthesis, and chemical synthesis].

44. (Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein [the] linkage between binding structure(s) and genetic and/or other identifying information comprises coded beads or polysomes.

45. (Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein [the] linkage between binding structure(s) and genetic and/or other identifying information comprises particles of filamentous phage or of any other virus.

46. (Amended) The method [Method] as claimed in claim 45, [characterized in that] wherein the filamentous phage is bacteriophage M13.

47. (Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the step of recovering [of] bound binding structures comprises [a] cleavage.

48. (Amended) The method [Method] as claimed in claim 47, [characterized in that] wherein the cleaved bound binding structure [the cleavage site] maintains [the] amplification ability.

49. (Twice Amended) The method [Method] as claimed in claim 45, [characterized in that] wherein the cleavage site is between the binding structure and a phage protein.

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

50. (Amended) The method [Method] as claimed in claim 49, [characterized in that] wherein the phage protein is [the] minor coat protein pIII.

51. (Amended) The method [Method] as claimed in claim 47, [characterized in that] wherein cleavage occurs at a protease recognition site [the cleavage site is a recognition site for a protease].

52. (Twice Amended) The method [Method] as claimed in claim 51 [47], [characterized in that] wherein the cleavage site is Ala-Ala-His-Tyr and the protease is Ala64-subtilisin.

53. (Twice Amended) The method [Method] as claimed in claim 51 [47], [characterized in that] wherein the cleavage site is Ile-Glu-Gly-Arg and the protease is blood clotting factor Xa.

54. (Amended) The method [Method] as claimed in claim 1, [characterized in that] wherein the step of recovering [recovery of] bound binding structures is effected by means of a chemically based elution.

55. (Amended) The method [Method] as claimed in claim 54, [characterized in that] wherein the elution is performed with an acid or alkaline solution[, such as triethylamine].

56. (Amended) The method [Method] as claimed in claim 6, [characterized in that] wherein the antibody is [the] a scFv C215 antibody fragment.

**Attachment to AMENDMENT AND REPLY dated October 19, 2001**

**Marked-up Claims 1-4, 6, 7, 9, 10, 17-27, 29, and 33-57**

57. (Amended) The method [Method] as claimed in claim 7, [characterized in that] wherein the [displayed] target structure is [the] an epitope on GA733-2 epithelial glycoprotein expressed in colorectal carcinoma.

Attachment to Reply and Amendment under 37 C.F.R. § 1.116



Diagram of "Comparison of Passive and Active Transport"

## Comparison of Passive and Active Transport.